Guidance for Industry

Providing Regulatory Submissions in Electronic Format — ANDAs

DRAFT GUIDANCE

This guidance document is being distributedfor commentpurposes only.

Comments and suggestions regarding this draft document should be submitted within 60 days of publication of the *Federal Register* notice announcing the availability of the draft guidance. Submit comments to the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fisher Lane, rm. 1061, Rockville, MD 20857. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register.*

For questions on the content of the draft document contact Ruth Warzala, 301-827-5845.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

October 2001
Electronic Submissions

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Additional copies are available from:

Office of Training and Communications
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Center for Drug Evaluation and Research
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Draft -- Not for Implementation

Guidance for Industry'

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This draft guidance, when finalized, will represent the Food and Drug Administration's current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statutes and regulations.

I. INTRODUCTION

This is one of a series of guidance documents intended to assist applicants making regulatory submissions in electronic format to the Center for Drug Evaluation and Research (CDER) and to the Center for Biologics Evaluation and Research (CBER). In some cases, guidance differs from CDER to CBER because of differences in the procedures and computer infrastructure in the Centers. The Agency will work to minimize these differences wherever possible.

This guidance discusses issues related to the electronic submission of abbreviated new drug applications (ANDAs) and supplements and amendments to those applications. This guidance should be used in conjunction with the guidance for industry on *Providing Regulatory Submissions in Electronic Format — General Considerations* (General Considerations guidance) (January 1999) and a guidance for industry on new drug applications (NDAs), *Providing Regulatory Submissions in Electronic Format — NDAs* (the NDA guidance) (January 1999). The General Considerations guidance addresses issues such as appropriate file formats, media, and submission procedures that are common to all submission types. The NDA guidance provides specific recommendations on the individual items on FDA Form 356h (Application to Market a New Drug, Biologic, or an Antibiotic Drug for Human Use). For a list of guidances that are under development on electronic submissions, see the General Considerations guidance.

Center policy is to encourage the submission and review of electronic ANDAs as described in this guidance. In January 1997, the Office of Generic Drugs (OGD) initiated a pilot program allowing some types of data and certain text information in electronic format to be submitted with the paper archive submission. The guidance on that program *(Preparing Data for Electronic Submission in ANDAs* (September 1999)) will be withdrawn when this guidance is finalized. We are currently working to harmonize data across the Centers and will include

[1] This guidance has been prepared by the Center for Drug Evaluation and Research (CDER) at the Food and Drug Administration.

On June 1, 1998, the President instructed all Federal agencies to ensure the use of plain language in new documents. This guidance reflects Agency efforts to comply with the plain language initiative.

additional recommendations on data submission in future versions of the NDA guidance. These recommendations will draw upon OGD's pilot program.

II. GENERAL ISSUES

Regulations in 21 CFR 3 14.94 provide general requirements for submitting ANDAs to CDER. Currently, FDA Form 356h outlines the components required in the submission of an abbreviated new drug application. This form is available on the Internet at (http://aosweb.psc.dhhs.gov/forms/fdaforms.htm). This section addresses some general considerations on the electronic submission of ANDAs.

A. Consistency With New Drug Application (NDA) Guidance

We have tried to make this guidance consistent with the NDA guidance wherever possible. This includes general issues about refusal to receive or file an application, providing the field copy, electronic signatures, and review aids, if submitted electronically.

B. Archival Copy

Once we have identified in public docket number 92-S-0251 that we can accept ANDAs in an electronic format, you have the option of providing the archival copy of the submission in electronic format as detailed in this guidance. If you decide to provide an ANDA in electronic format, you should provide the entire submission in electronic format. In addition, all subsequent supplements and amendments should be in electronic format. This will reduce confusion and improve review efficiency.

C. Review Copy

You are required to submit a review copy of an ANDA in addition to the archival copy (21 CFR 3 14.94(d)(2)). If you provide the archival copy in electronic format, you do not need to provide a separate review copy. For the copy of the analytical methods and descriptive information needed by FDA's laboratories to perform tests on samples of the proposed drug product and to validate the analytical methods (see 21 CFR 314.50(e)), if you provide the archival copy in electronic format, you should also provide the analytical methods information copy in electronic format. However, you do not need to provide additional copies of the analytical methods package.

D. Supplements and Amendments

The recommendations in this guidance apply equally to the original submission, supplements, and amendments to ANDAs.

E. Other Considerations

1. Page Numbering

You should only include page numbers within individual documents; pagination across all PDF documents is not necessary.

2. Indexing PDF Documents

You need not create full text indexes for ANDA electronic submissions.

3. Sending in the Electronic Submission to Be Archived

You should send the ANDA electronic regulatory submission to be archived to the CDER Central Document Room (CDR):

CENTRAL DOCUMENT ROOM
Center for Drug Evaluation and Research
Food and Drug Administration
12229 Wilkins Avenue
Rockville, MD 20852

CDER uses this submission to make other copies as needed. We duplicate the electronic files on tape to create an archival copy and load the files onto a network server to create a read-only copy for the reviewer. *Note: The procedure for handling paper submissions is unchanged from the past.*

4. The Type of Media That Should Be Used

Refer to the General Considerations guidance for information on media

5. Preparing the Media

Refer to the General Considerations guidance for general information on preparing the media.

The first binder with electronic media should include only a paper copy of the cover letter for the submission, a paper copy of FDA Form 356h, and the electronic media for archiving. On page 1 of FDA Form 356h, note that the application is in "ELECTRONIC" format.

Please attach labels to the media, and if using CDs, also attach labels to the CD jewel cases. The media should be labeled with the following:

ANDA ELECTRONIC SUBMISSION
ANDA Number (if available)

Company name
Drug Product Name and Strength(s)
Submission type (original, amendment, supplement)
Submission date
Disk/CD-ROM (the total number submitted such as Disk # of #)
Point of Contact (name and telephone number of person with knowledge of the electronic submission)

F. Questions on ANDA Electronic Submissions

You can direct questions regarding the preparation of submissions in electronic format for ANDAs to the Electronic Submissions Technical Support ESUB@CDER.FDA.GOV.

III. ORGANIZING THE MAIN FOLDER

All documents and data files for the electronic archival copy should be placed in a main folder using *ANDA* as the folder name.

A. Folders

Inside the main folder, there should be five folders: *labeling, cmc, hpbio, crt, crf,* and *other*. The documents and data files should be organized by the ANDA items described on page 2 of FDA Form 356h. Each item has an assigned subfolder where documents and data files that belong to the item should be placed. See Table 1 below for the items and folder organization.

Table 1. Items of an ANDA as Described on FDA Form 356h

Item	Description	Folder name
	Cover letter	ANDA
	Regulatory basis of submission	ANDA
2	Labeling	labeling
4	Chemistry	cmc
6	Human pharmacokinetics (Bioequivalence)	hpbio
11	Case report tabulations	crt
12	Case report forms	crf
14	Patent certification	other
16	Debarment certification	other
17	Field copy certification	other
19	Financial information	other
20	Other	other

B. Cover Letter

You should provide the cover letter as described in the NDA guidance.

C. Basis for the ANDA submission

You must provide information for the comparison of the generic drug and the reference listed drug (section 505(j)(2)(A) of the Federal Food, Drug, and Cosmetic Act; 21 CFR 3 14.94(a)(3)), conditions for use (21 CFR 314.94(a)(4)), active ingredients (21 CFR 3 14.94(a)(5)), and route of administration (21 CFR 3 14.94(a)(6)). You should provide this information in a single PDF file named *regbasis.pdf* and place it in the *ANDA* folder. This document should have a table of contents listing each one of the required items listed above. As part of the comprehensive table of contents, you should provide bookmarks to each item listed in the table of contents.

D. FDA Form 356h

You should provide the FDA Form 356h as described in the NDA guidance.

E. ANDA Table Of Contents (Index)

Inside the main ANDA folder, you should provide a table of contents for the submission named *andatoc.pdf*. See item 1 below for additional information.

IV. ORGANIZING THE ELECTRONIC SUBMISSION

The submission should contain the documents and data files for the appropriate items listed on FDA Form 356h. The guidance for providing each item in electronic format follows.

A. Item 1: Table of Contents

You should provide the table of contents for the ANDA as described in the NDA guidance. Name the table of contents *andatoc.pdf*.

You need not include items 5 (Nonclinical pharmacology and toxicology), 7 (Clinical Microbiology), 8 (Clinical data), 9 (Safety update report), 10 (Statistical section), 13 (Patent information), 15 (Establishment description), or 18 (User Fee Cover Sheet), because this information is not part of an ANDA. An example of the table of contents for ANDA 012345 is in Table 2.

Table 2. Example: Table of Contents for ANDA 012345

Description	Electronic Archive Copy Folder Name
Table of contents	ANDA
Labeling	labeling
Chemistry	cmc
Bioequivalence	hpbio
Case report tabulations	crt
Case report forms	crf
Patent certification	other
Debarment certification	other
Field copy certification	other
Financial disclosure	other
List other files here	other

B. Item 2: Labeling

Labeling is item 2 on page 2 of FDA Form 356h. You should provide the labeling as described in the NDA guidance.

In addition to the files described in the NDA guidance, you must provide a statement that your proposed labeling is the same as the labeling of the reference listed drug except for differences explained in the annotated comparison of labeling (21 CFR 314.94(a)(8)(iii)). You should provide this statement in a PDF file named *compare.pdf* and place it in the *labeling* folder.

You must also provide a copy of the approved labeling text for the listed drug referred to in the ANDA, if it relies on a reference listed drug (3 14.94(a)(8)(i)). You should name the *file listed.pdf* and place it in the *labeling* folder.

C. Item 4: Chemistry, Manufacturing, and Controls (CMC)

The chemistry, manufacturing, and controls section is item 4 on page 2 of FDA Form 356h. You should provide the information as described in the NDA guidance.

D. Item 6: Human Pharmacokinetics and Bioavailability

The bioequivalence study reports including the assay validation studies and in vivo in vitro dissolution studies, are included under item 6 on page 2 of FDA Form 356h. You should provide the information as described in the NDA guidance.

If you provide a waiver for in vivo studies, provide it as a single PDF file called *waiver.pdf* and place it in the *hpbio* folder. This file should contain all information required to support a waiver.

You should provide any other items pertinent to the bioequivalence submission as separate PDF files and place them in the *hpbio* folder. There should be a hypertext link from the hpbio table of contents directly to these files.

E. Item 11: Case Report Tabulations (CRTs)

CRTs are item 11 on page 2 of FDA Form 356h.

You should provide the data from the various studies in a series of datasets. You should follow the NDA guidance on the format and documentation of the datasets. The NDA guidance also describes how to provide a table of contents for the datasets. Place them in the *crt* folder for processing efficiency.

F. Item 12: Case Report Forms (CRFs)

CRFs are item 12 on page 2 in FDA Form 356h.

You should follow the guidance provided in the NDA guidance for submitting case report forms.

G. Other Items:

You should follow the guidance provided in the NDA guidance for submitting the debarment certification (item 16), field copy certification (item 17), and financial disclosure information (item 19).

Provide the information pertaining to the patent certification (2 1 CFR 3 14.94(a)(12)) and exclusivity (2 1 CFR 3 14.94(a)(3)) in a single PDF file named *patcert.pdf* and place it in the *other* folder.

Provide any other items pertinent to the submission as separate PDF files and place them in the *other* folder. There should be a hypertext link from the submission table of contents directly to these files.

The Agency is developing procedures for the submission of electronic signatures. Until those procedures are in place, a signed paper certification or declaration must be accompany the electronic submission wherever a handwritten signature is currently required (3 14.94(a)(1)).